IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant(s):	D. Wade Walke, *et al.*	Group Art Unit: 1652
Application No.:	09/783,320	Examiner: D.M. Ramirez
Filed:	02/15/01	
Title:	Novel Human Kinases and Polynucleotides Encoding the Same	Atty. Docket No. LEX-0137-USA

APPEAL BRIEF

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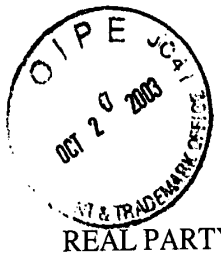
Commissioner for Patents
Alexandria, VA 22313



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Sir:

Appellants hereby submit an original and two copies of this Appeal Brief to the Board of Patent Appeals and Interferences ("the Board") in response to the Final Office Action mailed December 17, 2002. The Notice of Appeal was timely submitted on March 11, 2003, and was received in the Patent and Trademark Office ("the Office") on March 18, 2003. This Appeal Brief is timely submitted in light of the concurrently filed Petition for an Extension of Time of five months to and including October 18, 2003, which falls on a Saturday and is therefore extended to Monday October 20, 2003, and authorization to deduct the fee as required under 37 C.F.R. § 1.17(a)(2) from Appellants' Representatives' deposit account. The Commissioner is also authorized to charge the fee for filing this Appeal Brief (**$165.00**), as required under 37 C.F.R. § 1.17(c), to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

Appellants believe no fees in addition to the fee for filing the Appeal Brief and the fee for the extension of time are due in connection with this Appeal Brief. However, should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason related to this communication, the Commissioner is authorized to charge any underpayment or credit any overpayment to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

I. REAL PARTY IN INTEREST

The real party in interest is the Assignee, Lexicon Genetics Incorporated, 8800 Technology Forest Place, The Woodlands, Texas, 77381.

II. RELATED APPEALS AND INTERFERENCES

Appellants know of no related appeals or interferences.

III. STATUS OF THE CLAIMS

The present application was filed on February 15, 2001, claiming the benefit of U.S. Provisional Application Numbers 60/183,582 and 60/184,014 which were filed on February 18, 2000, and February 22, 2000, respectively. As filed, the present application included original claims 1-10. A Restriction and Election Requirement was issued by the Office on November 28, 2001(Paper No. 8), in which the Examiner determined that the original claims represented into six separate and distinct inventions. In the Response to the Restriction Requirement, submitted to the Office on December 28, 2001, Appellants elected, with traverse, the claim of the Group II (Claim 4) for prosecution on the merits. Appellants further elected, pursuant to 35 U.S.C. § 112, the species of SEQ ID NO: 3/4 for initial examination on merits. Appellants canceled claims 1-3 (Group I invention) and 6-10 (Group IV,V,VI inventions) without prejudice or disclaimer as being drawn to a non-elected invention. A First Official Action, was issued on May 22, 2002 ("the First Action": Paper No.11), claim 4 was rejected under 35 U.S.C. § 101, due to an alleged lack of patentable utility. Claim 4 was also rejected under 35 U.S.C. § 112, first paragraph, as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility and claim 5 was withdrawn from further consideration by examiner, 37 CFR1.142(b), as being drawn to a non-elected invention. In a response to the First Official Action, submitted to the Office on September 23, 2002 ("response to the First Action"), Appellants added new claims 11-14 were added to better claim the present invention. A Second and Final Official Action, was issued on December 17, 2002 (the "Final Action"), in which rejection of claims 4, 11, and 12 were maintained under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph, claims 13-14 are withdrawn from further consideration by examiner, 37 CFR1.142(b), as being drawn to a non-elected invention (Claim 5). In a response to the Final Action, submitted on April 17, 2003 (Response to the Final Action"), Appellants again addressed the outstanding rejections of the pending claims with regards to the continuing rejection under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph. An Advisory Action ("the Advisory Action") was mailed on May 20, 2003, maintaining the rejection of claims 4, 11 and 12 under 35 U.S.C. § 101, as allegedly lacking a patentable utility, rejection of claims 4, 11 and 12 were also maintained under 35 U.S.C. § 112, first paragraph, as one skilled in the art clearly would not

know how to use the skilled invention, the fact that claims 5, 13 and 14 had been withdrawn from further consideration by examiner, 37 CFR1.142(b), as being drawn to a non-elected invention, was reiterated. A Notice of Appeal was filed by Appellants on March 11, 2003. A copy of the appealed claims is included below in the Appendix (Section IX).

IV. STATUS OF THE AMENDMENTS

For the purposes of Appeal Appellants believe that no additional outstanding amendments exist.

V. SUMMARY OF THE INVENTION

The present invention relates to Appellants' discovery and identification of novel human sequences that encode a human kinase protein. Also disclosed is the tissue expression pattern of these sequences (page 3, lines 14-20). The specification details a number of uses for the presently claimed sequences, including the detection and diagnosis of human diseases such as, *inter alia*, obesity, high blood pressure, connective tissue disorders and infertility (specification at page 12, line 33). Additional uses for the sequences of the present invention described in the specification include assessing temporal and tissue specific gene expression patterns (specification at page 6, line 28-30), particularly using a high throughput "chip" format (specification at page 6 through page 8), mapping the sequences to a specific region of a human chromosome and identifying protein encoding regions (specification at page 11, lines 11-17), determining the genomic structure (specification at page 11, line 11), and in diagnostic assays such as forensic analysis, human population biology and paternity determinations (see, for example, the specification from page 8, lines 12-14). Thus, Appellants have described sequences encoding a novel human kinase protein, a class of proteins which are well known to those of skill in the art and have well accepted utility.

VI. ISSUES ON APPEAL

1. Do claims 4, 11 and 12 lack a patentable utility?
2. Are claims 4, 11 and 12 unusable by a skilled artisan due to a lack of patentable utility?

VII. GROUPING OF THE CLAIMS

For the purposes of the outstanding rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, the claims will stand or fall together.

VIII. ARGUMENT

A. Do Claims 4, 11 and 12 Lack a Patentable Utility?

The Final Action rejected and the Advisory Action maintained the rejection of claims 4, 11 and 12 under 35 U.S.C. § 101, as allegedly lacking a patentable utility due to not being supported by either a specific and substantial utility or a well-established utility, this rejection is maintained in the Advisory Action.

Appellants have described the nucleic and amino acid sequences that encode a human kinase protein, and their tissue expression pattern. Appellants' assertion that the sequences of the present invention encode a human kinase protein is apparent throughout the specification as filed (at least in the title, in Section 2 and more specifically on page 16, lines 14 -17). The sequences of the present invention encode human kinase protein, a variant of NEK-1.

First, as set forth in the response to the First Action and the response to the Final Action, Appellants would like to invite the Board's attention to the fact that a sequence that is 96.343% identical at the amino acid level over the entire length of the described sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists wholly unaffiliated with Appellants as *Homo sapiens* (Human) SERINE/THREONINE KINASE NEK-1 (GenBank (Swissprot) accession no. Q96PY6 and International Protein Index (IPI) accession number IPI00044749.2; alignment and information provided as **Exhibit A**). Appellants note, that as stated on the last line of page 4 of the Advisory Action, these numbers represent the same protein. The GenBank accession no.(Q96PY6) was provided along with the IPI entry and alignments of both with SEQ IDNO:4 of the present invention, when in response to the Appellants' response to

the First Action the Examiner appeared to be unable to access the IPI public database. This information was provided to make it clear that they represented the same protein and that, as asserted in both responses, the sequences of the present invention represent a variant of the human kinase protein, NEK-1.

Also as set forth in the response to the First Action, NEK-1 is known to the art, see for example, Letwin, et al., "A mammalian dual specificity protein kinase, Nek1, is related to the NIMA cell cycle regulator and highly expressed in meiotic germ cells", EMBO J, Oct;11(10):3521-31, 1992, abstract presented as **Exhibit B**). Studies in homozygous NEK-1 mutant animals indicated a phenotype that indicates that the NEK1 protein participates in signaling pathways to regulate cellular processes and identified a role for Nek1 in the kidney and open a new avenue for studying cystogenesis and identifying possible modes of therapy (Upadhya, *et al.*, "Mutations in a NIMA-related kinase gene, Nek1, cause pleiotropic effects including a progressive polycystic kidney disease in mice", Proc Natl Acad Sci USA, Jan 4;97(1):217-21, 2000: abstract presented as **Exhibit C**). These references clearly supports Appellants' position that the invention has utility and a disease association. Given this clear evidence that those skilled in the art have independently accepted the utility described in the present specification, there can be no question that Appellants' asserted utility for the described sequences is "credible." As such, the scientific evidence of identity at both the amino acid and nucleic acid levels clearly establishes that those of skill in the art would recognize the sequences of the present invention as human kinase, a protein with well known function. Therefore, Appellants have described a utility in full compliance with the provisions of 35 U.S.C. section 101, and the Examiner's rejection should be overturned.

In contrast the Advisory Action, however, reiterates the Examiner's position that structural homology is not sufficient to assign function (page 5, second paragraph) and provides additional citations to support of this position. The Examiner had previously cited Bork (Genome Research *10*:398-400, 2000) as supporting the proposition that prediction of protein function from homology information is somewhat unpredictable and had directed attention to page 399, on which the author notes the limitations of various methods of analysis. It is of interest that in his "analysis" Bork often uses

citations to many of his own previous publications, an interesting approach. ' My position is supported by my previous disclosures of my position.' If Bork's position is supported by others of skill in the art, one would expect that he would reference them rather than himself to provide support for his statements. Given that the standard with regard to obtaining U.S. patents is those of skill in the art, this observation casts doubt on the broad applicability of Bork's position. It should also be noted that in Table 1, on page 399, in which selected examples of prediction accuracy are presented, that the reported accuracy of the methods which Appellants have employed are, in fact, very high. While nowhere in Bork is there a comparison of the prediction accuracy based on the percentage homology between two proteins or two classes of proteins, " Homology (several methods)" is assigned an accuracy rate of 98% and "Functional features by homology" is assigned an accuracy rate of 90%. Given that these figures were obtained based on what is at least a 4 year old analysis, these high levels of accuracy would appear to support rather than refute Appellants' assertions in the present case. Additionally Bork even states (on page 400, second column, line 17) that " However, there is still no doubt that sequence analysis is extremely powerful". In summary, it is clear that it is not Bork's intention to refute the value of sequence analysis but rather he is indicating that there is room for improvement. The Examiner had also cited Broun *et al.* (Science *282*:1315-1317, 1998) and in the Advisory Action adds citations to Van de Loo *et al.* (Proc. Natl. Acad. Sci. USA *92*:6743-6747, 1995), Seffernick *et al.*, (J. Bacterol; 183(8):2405-2410, 2001) and Witkowski *et al.*, (Biochemisty 38:11643-11650, 1999) as teaching that prediction of function based on homology is unpredictable. However, each of these papers cite only single rare examples, of non-kinases, where function based on sequence homology would have been proven to be incorrect. A few select examples out of the thousands of predictions of function based on homology that exist in the art is hardly indicative of a high level of uncertainty, and thus also does not support the alleged lack of utility. In the present case, the Examiner has taken what has become a common approach by citing the occasional journal article to support an allegation of a lack of utility, the PTO has repeatedly attempted to deny the utility of nucleic acid sequences based on a small number of publications that call into doubt prediction of protein function from homology information and the usefulness of bioinformatic predictions, of which these

articles are merely the latest examples. Appellants agree that there is not 100% consensus within the scientific community regarding prediction of protein function from homology information, and further agree that prediction of protein function from homology information is not 100% accurate. However, Appellants respectfully point out that the lack of 100% consensus on prediction of protein function from homology information is irrelevant to the question of whether the claimed nucleic acid sequence has a substantial and specific utility, and that 100% accuracy of prediction of protein function from homology information is **not the standard** for patentability under 35 U.S.C. § 101. Appellants respectfully point out that, as discussed above, the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be **believable**. Appellants submit that the overwhelming majority of those of skill in the relevant art would **believe** prediction of protein function from homology information and the usefulness of bioinformatic predictions to be powerful and useful tools, as evidenced by extensive number of journal articles (which support Appellants' assertion that the overwhelming majority of those of skill in the art place a high value on prediction of protein function from homology information and the usefulness of bioinformatic predictions), and would thus **believe** that Appellants' sequence is a kinase protein, (NEK-1) whose function has been described. As **believability** is the standard for meeting the utility requirement of 35 U.S.C. § 101, and **not** 100% consensus or 100% accuracy, Appellants submit that the present claims must clearly meet the requirements of 35 U.S.C. § 101.

Even the **PTO itself** does not require 100% identity between proteins to establish functional homology. The Examiner's position that homology of SEQ ID No:1 to a known DNA molecule with a known function does not endow SEQ ID NO:1 with the function is contrary to Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when there is no reason to doubt the asserted utility of a full length sequence (such as the presently claimed sequence) that has a similarity score of 95% to a protein having a known function. In the Analysis portion of Example 10 it states that "Based on applicant's disclosure and the results of

the PTO search, there is no reason to doubt the assertion that SEQ ID NO:2 encodes a DNA ligase. Further DNA ligases have a well-established use in the molecular biology art based on this class of proteins ability to ligate DNA. .....Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed..... Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made."

Clearly evidence supports Appellants' assertions that the sequences of the present invention encode a novel human kinase protein (specifically NEK-1), a class of proteins for which there is a well established utility that is recognized by those of skill in the art. The present case is identical to that presented in Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55). In the present case it is clear that the sequences of the present invention encode novel human kinase. The Final Action dismisses Appellants' continued assertions that the protein of the present invention is a protein kinase and that as a kinase protein, their function is both well known and implied to those of skill in the art. Protein kinases have a well-established use in the molecular biology art based on this class of proteins ability to phosphorylate proteins at serine and threonine residues, (this utility is so well known that U.S. Patent No. 5,817,479 has issued on human kinase fragments). Thus, according to the guidelines "Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed...Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made." Thus the rejection of the presently claimed invention under a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph utility rejection should be overruled.

Thus, the skilled artisan would readily appreciate the utilities asserted by Appellants' regarding the role of the proteins encoded by sequences of the present invention, including those associated with diseases that have been linked to the novel human kinase proteins. Therefore, the present utility rejection must fail. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the

art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

The Advisory Action disregards Appellants' assertions regarding the use of the presently claimed polynucleotides on DNA gene chips, based on the position that such a use would allegedly be generic. Further, these Actions seem to be requiring Appellants to identify the biological role of the nucleic acid or function of the protein encoded by the presently claimed polynucleotides before the present sequences can be used in gene chip applications that meet the requirements of § 101. Appellants respectfully point out that knowledge of the exact function or role of the presently claimed sequence is not required to track expression patterns using a DNA chip. As set forth in Appellants First Response, given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications.

However, clearly given the extensive utility described above for the kinase molecules encoded by the sequences of the present invention and evidence that the claimed sequences provide a specific marker of the gene encoding the human kinase NEK-1and provide a unique identifier (the sequence specifically identifies the gene) of the corresponding gene in the human genome. Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing NEK-1 kinase gene expression using, for example, DNA chips, as the specification details at least on page 5, line 30 through page 6, line 33. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, exemplified by U.S. Patent Nos. 5,445,934 (**Exhibit D**), 5,556,752 (**Exhibit E**), 5,744,305 (**Exhibit F**), as well as more recently issued U.S. Patent Nos. 5,837,832 (**Exhibit G**), 6,156,501 (**Exhibit H**) and 6,261,776 (**Exhibit I**).

The Board is further requested to consider that, given the huge expense of the drug discovery process, even negative information has great "real world" practical utility. Knowing that a given gene is not expressed in medically relevant tissue provides an informative finding of great value to industry by allowing for the more efficient deployment of expensive drug discovery resources. Such practical considerations are equally applicable to the scientific community in general, in that time and resources

are not wasted chasing what are essentially scientific dead-ends (from the perspective of medical relevance). Clearly, compositions that enhance the utility of such DNA gene chips, such as the presently claimed sequences encoding the human kinase NEK-1 must in themselves be useful. Moreover, the presently described kinase (NEK-1) provides uniquely specific sequence resources for identifying and quantifying full length transcripts that were encoded by the corresponding human genomic locus. Accordingly, there can be no question that the described sequences provide an exquisitely specific utility for analyzing gene expression.

The utility of the sequences of the present invention are further enhanced by the description in the specification of tissues expressing the sequences of the present invention (Page 3, lines 14-20). These teachings along with the above evidence that the molecules of the present invention encode a kinase protein of known function, clearly demonstrates the outstanding utility of the sequences of the present invention in DNA chip expression analysis.

Still further, as only a small percentage of the genome (2-4%) actually encodes exons, which in turn encode amino acid sequences. Thus, not all human genomic DNA sequences are useful in such gene chip applications. This further discounts the Examiner's position that such uses are "generic". The present claims clearly meet the requirements of 35 U.S.C. § 101. It has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971).

Additional evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company, Rosetta Inpharmatics, was viewed to have such "real world" value that it was acquired by large pharmaceutical company, Merck & Co.,

for substantial sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304; **Exhibit J**). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153; **Exhibit K**). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

Given the physiologic activity and importance of kinase proteins and NEK-1 as known to those of skill in the art, those of skill in the art would readily appreciate the importance of tracking the expression of the genes encoding the described proteins. The use of the claimed polypeptide in an array for screening purposes Appellants respectfully point out that nucleic acid sequences have the greatest specific utility in gene chip applications once the role of the sequence has been identified, as have tissues of interest, as in the present case. Once the role of the particular nucleic acid is known, the level of gene expression has and even greater significance. By identifying the physiological activity role of the claimed sequence, the claimed sequence has a far greater utility in gene chip applications that just any random piece of DNA. Appellants respectfully submit that **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, is distinct from the requirement for a **unique** utility, which is clearly an improper standard. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not

grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Therefore, just because other nucleic acid sequences find utility in gene chip applications does not mean that the use of Appellants' sequence in gene chip applications is not a specific utility. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer and bacterial or viral infections, just to name a few particular examples, because examples of each of these have already been described and patented. All batteries have the exact same utility - specifically, to provide power. All automobile tires have the exact same utility - specifically, for use on automobiles. All golf balls and golf clubs have the exact same utility - specifically, use in the game of golf. All cancer treatments have the exact same utility - specifically, to treat cancer. All anti-infectious agents have the exact same broader utility - specifically, to treat infections. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Further evidence of utility of the presently claimed polynucleotide, although only one is needed to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), is the specific utility the present nucleotide sequence has in determining the genomic structure of the corresponding human chromosome (specification at page 11, lines 11-17), for example mapping the protein encoding regions as described in the specification (page 11, lines 11-14) and evidenced below. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the

gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequence. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Only a minor percentage of the genome actually encodes exons, which in turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* defines that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Appellants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence supporting the Appellants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra at* pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article.

As still further evidence supporting Appellants assertions of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome and identification of functionally active intron/exon splice junctions is the information provided in **Exhibit L**. This is the result of a blast analysis using SEQ ID NO:3 of the present invention when compared to the identified human genomic sequence. By doing this, one is able to identify the portions of the genome that encode the present invention. As these regions of the genome are non-contiguous, this is indicative of individual

exons. This result indicates that the sequence of the present invention is encoded by 31 exons spread non-contiguously along a region of human chromosome 4, which is represented by 5 adjacent BAC clones, AC116621,AC084724, AC116615, AC11643 and AC11642. Thus clearly one would not simply be able to identify the 31 protein encoding exons that make up the sequence of the present intention, nor to map the protein encoding regions identified specifically by the sequences of the present invention without knowing exactly what those specific sequences were. Additionally, it should be noted that the human NEK-1 kinase gene has since been mapped by those unaffiliated with Appellants to the same region of human chromosome 4 (4q32.3). This further supports Appellant's position that the sequences of the present invention encodes a variant of the human NEK-1 kinase.

The Examiner states in the Advisory Action (page 6 last paragraph- page 7) that it is unclear how the determination of the number of exons has been made and that this does not represent empirical data. Appellants respectfully disagree and note that those of skill in the art would readily recognize that when a sequence encoding an expressed gene is mapped onto know genomic sequence, that those area in which the sequence is non-contiguously mapped represent exon/intron boundries and that the presence of an exon/intron boundry represents either the beginning or the end of an exon and thus the number of discontinuous genomic sequence (exons) that are linked (spliced) during expression, represents the number of exons encoding the expressed protein encoding sequence. Clearly this provided empirical evidence supporting Appellants assertions of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome that encodes the kinase (NEK-1) of the present invention as well as the ability of such sequences to be used to identify functionally active intron/exon splice junctions.

Appellants respectfully submit that the question of utility is a straightforward one. As set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d

1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

In *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted. In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (C.C.P.A. 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Finally, with regards to the issue of due process, while Appellants are well aware of the new Utility Guidelines set forth by the USPTO, Appellants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Appellants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Board is invited to review U.S. Patent Nos. 5,817,479 (**Exhibit M**), 5,654,173 (**Exhibit N**), and 5,552,281 (**Exhibit O**; each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (**Exhibit P**; which includes no

working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section VIII(B), below), Appellants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Appellants agree that each application is examined on its own merits, Appellants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Given the rapid pace of development in the biotechnology arts, it is difficult for the Appellants to understand how an invention fully disclosed and free of prior art at the time the present application was filed, could somehow retain *less* utility and be *less* enabled than inventions in the cited issued U.S. patents (which were filed during a time when the level of skill in the art was clearly lower). Simply put, Appellants' invention is *more* enabled and retains *at least as much* utility as the inventions described in the claims of the U.S. patents of record. Thus, holding Appellants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

Thus in summary, Appellants have described novel nucleic and amino acid sequences that encode a human kinase (NEK-1) and their tissue specific expression pattern. Furthermore, the sequences of the present invention encode the human kinase (NEK-1), a protein of well recognized function. The present situation directly tracks Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when the full length sequence of the invention encodes a protein that has a well known function. Furthermore this response has described a series of additional substantial, specific, credible and well-established utilities for the present invention in addition to those described in Appellants' many previous responses. Therefore, Appellants submit that as the presently claimed sequence molecules have been shown to have a

substantial, specific, credible and well-established utility, the rejection of the claims under 35 U.S.C. § 101 has been overcome. Thus, Appellants respectfully request that the rejection be overruled.

B. Are Claims 4, 11 and 12 Unusable Due to a Lack of Patentable Utility?

The Final Action next rejects claims 4, 11 and 12 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by either a clear asserted utility or a well-established utility.

The arguments detailed above in **Section VIII(A)** concerning the utility of the presently claimed sequences are incorporated herein by reference. As the Federal Circuit and its predecessor have determined that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph, have the same basis, specifically the disclosure of a credible utility (*In re Brana, supra*; *In re Jolles*, 628 F.2d 1322, 1326 n.11, 206 USPQ 885, 889 n.11 (CCPA 1980); *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971)), Appellants submit that as claims 4, 11 and 12 have been shown to have "a specific, substantial, and credible utility", as detailed in **Section VIII(A)** above, the present rejection of claims 4, 11 and 12 under 35 U.S.C. § 112, first paragraph, cannot stand.

Appellants therefore submit that the rejection of claims 4, 11 and 12 under 35 U.S.C. § 112, first paragraph, must be overruled.

IX. APPENDIX

The claims involved in this appeal are as follows:

4. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO: 4.

11. An expression vector comprising a nucleic acid sequence of Claim 4.

12. A cell comprising the expression vector of Claim 11.

X. CONCLUSION

Appellants respectfully submit that, in light of the foregoing arguments, the Final Action's conclusion that claims 4, 11 and 12 lack a patentable utility and are unusable by the skilled artisan due to a lack of patentable utility is unwarranted. It is therefore requested that the Board overturn the Final Action's rejections.

Respectfully submitted,

October 20, 2003
Date

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